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DETERMINATION OF BACTERITROPIC CONTENT OF ANTIMENINGOCOCCIC SERUM.

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There are several possible methods for testing antimeningococcus serum for its content in immune antibodies, but none of them is considered entirely satisfactory. The agglutination reaction is the simplest of these tests and it is the one most commonly applied. Inasmuch as the part which agglutinins may play in the therapeutic activity of the serum is unknown, a high content of agglutinins in a serum does not give assurance that the serum in question would be efficacious in the treatment of disease. Investigators of serum immunized against various kinds of pathogenic organisms have shown that a high agglutinin content is not always paralleled with a high content of other known antibodies.

The complement fixation reaction is also commonly used for testing antimeningococcic serum, but this test is not entirely satisfactory for a similar reason, and also on account of the great complexity of the test. Neither the phenomenon of agglutination, nor that of fixation of complement (since complement is lacking in the cerebrospinal fluid) appears to be a necessary part of the human defense in cerebrospinal meningitis.

Judged by the picture of the disease, it appears that those antibodies which act upon the invading organisms in such a manner that they are prepared for ingestion by the leucocytes probably play an important part in the therapeutic activity of the serum. If that is true, then a quantitative determination of the antibodies promoting phagocytosis should give some indication of the therapeutic value of a serum. Heretofore a reliable method for determining the phagocytic antibodies has not been described, and the "opsonic" test, as it was called, was rejected because experienced laboratory workers could not obtain consistent results.

In view of the importance of a reliable test by which to judge the large quantities of antimeningococcus serum needed to combat the outbreaks of miningitis in the army camps, a study of the phagocytosis-promoting bodies of antimeningococcic serum was undertaken as a war emergency problem. Before a satisfactory method for carrying out this test had been developed, the signing of the armistice relieved the urgency for haste in perfecting a new method; consequently there was undertaken a more comprehensive study of the meningococci in our collection than was at first contemplated.

It was found that the important phagocytic antibodies of antimeningococcic serum are not the labile opsonins which depend upon complement for their activity, but they are the more stable bacteriotropins. Contrary to the report of Kolmer (1)[1] and his associates, who recommended the addition of complement to antimeningococcus serum before using it for treatment, there was never observed any reactivating effect when complement was added to commercial serum.

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[1] Number indicates reference cited.

The early investigators of meningococcus serum reported that some of their strains were resistant to phagocytosis, and would not respond to treatment with immune serum. They attributed such a resistance to the inherent properties of certain strains. But it is now evident that the strains were found to be resistant because those investigators expected a serum immunized against one strain of meningococcus to react with every other strain of meningococcus, whereas it will react with only such strains as belong to the same specific group.

Dopter (2)[1] found two groups of meningococci distinguishable by their agglutinin reactions. Gordon (3)[1] also studied the agglutinin reactions of meningococci and grouped the epidemic strains in England into four types.

Similarly, I have found distinct groups of meningococci distinguishable by their tropin relationship. Four such groups were distinguishable which have been designated R, S, T, and U. A fifth group, Z, is made up of organisms which are more or less closely related to all the other groups.

To some extent there is a coincidence between the agglutinin types and the tropin groups. Group R includes the majority of strains of Gordon's Type I. It also includes the majority of strains of Type III and a few strains of other types. Group S includes the majority of strains of Type II, and a few strains of other types. Group T is a small group made up of strains of various types. Group U was represented by a single strain in our collection.

Groups R, S, T, and U are well defined. Only a few strains belonging to these groups were found to have any tropin relationship with the other groups. For example, a strain of Group S will show no reaction in a Group R serum. Obviously, so long as these groups were unrecognized in phagocytic studies and a serum obtained by immunizing against one strain of meningococcus was expected to react with every other strain of meningococcus, inconsistent results were inevitably reported.

No strain of meningococcus was found to be resistant to phagocytosis after treatment with specific tropins, and every tested strain was found to possess tropinogenic powers. But those unqualified statements do not apply to all strains which have been maintained for a long time under artificial conditions. Strains in our collection have been observed to weaken in their tropinogenic powers, and also in their power of response to specific tropins. The entire loss of both properties has been observed in a few strains.

There is a practical significance in the loss of antibody producing properties by strains of meningococci after long artificial cultivation.

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[1] Number indicates reference cited.

Such strains can not be relied upon as antigens for the production of serum for therapeutic purposes.

It has been the common observation of investigators that the agglutinin content of immune serum is not always paralleled by the tropin content. That was found to be the case with antimeningococcic serum. In the majority of serums prepared for experimental purposes a good production of agglutinins was found to be accompanied by a good production of tropins; but strains which had lost their tropinogenic power were shown to possess good agglutinogenic properties. On the other hand, strains with a poor agglutinogenic power were found to produce serum with a good tropin content.

The two antibodies are affected differently by adverse conditions. The agglutinins were destroyed at a lower temperature than the tropins; but some other adverse conditions were found to destroy the tropins more readily than the agglutinins.

Thus it was shown that the two antibodies are independent of one another in their characteristic effects on meningococci. It is therefore not to be expected that a commercial serum containing a good content of agglutinins will always contain a good content of tropins.

One hundred and twenty-eight commercial serums have been examined for their content of tropins specific for Groups R and S, and the results were compared with the agglutination reactions of those serums as determined at the Hygienic Laboratory.

The two tests agreed in the case of about 70 per cent of the serums, but for the remaining serums the results were discordant; so that a serum which was rejected by the agglutinin test would have passed if judged by the tropin test alone, or vice versa In the case of some of the serums for which the results were discordant the content of both antibodies was near the lower limit—that of the one lying just above and that of the other lying just below the arbitrary standard. But a few of the serums showed a high content of the one antibody and a low content of the other.

The tropin test has proved to be a workable test, giving results as consistent as can be expected in such a complicated biological reaction. Retests on the same serum have shown practically the same content of tropins for the various groups of meningococci as in the original tests.

The full report, including tables giving the data upon which the above conclusions were based, is now in manuscript, and will be published in a Hygienic Laboratory bulletin.

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